

Organic anionic transporter

1. Organic Anion Transporters (OAT, SLCO, OATP)



- **Ionic agents** generally exhibit low passive membrane permeability, resulting in their poor bioavailability.
- An **organic anion-transporter** is a membrane transport protein or 'transporter' that transports organic anions across the cell membrane.
- These are present in the lipid bilayer of the cell membrane. OATs belong to the Solute Carrier Family (SLC), more specifically the Solute Carrier Organic Anion (SLCO) gene subfamily.



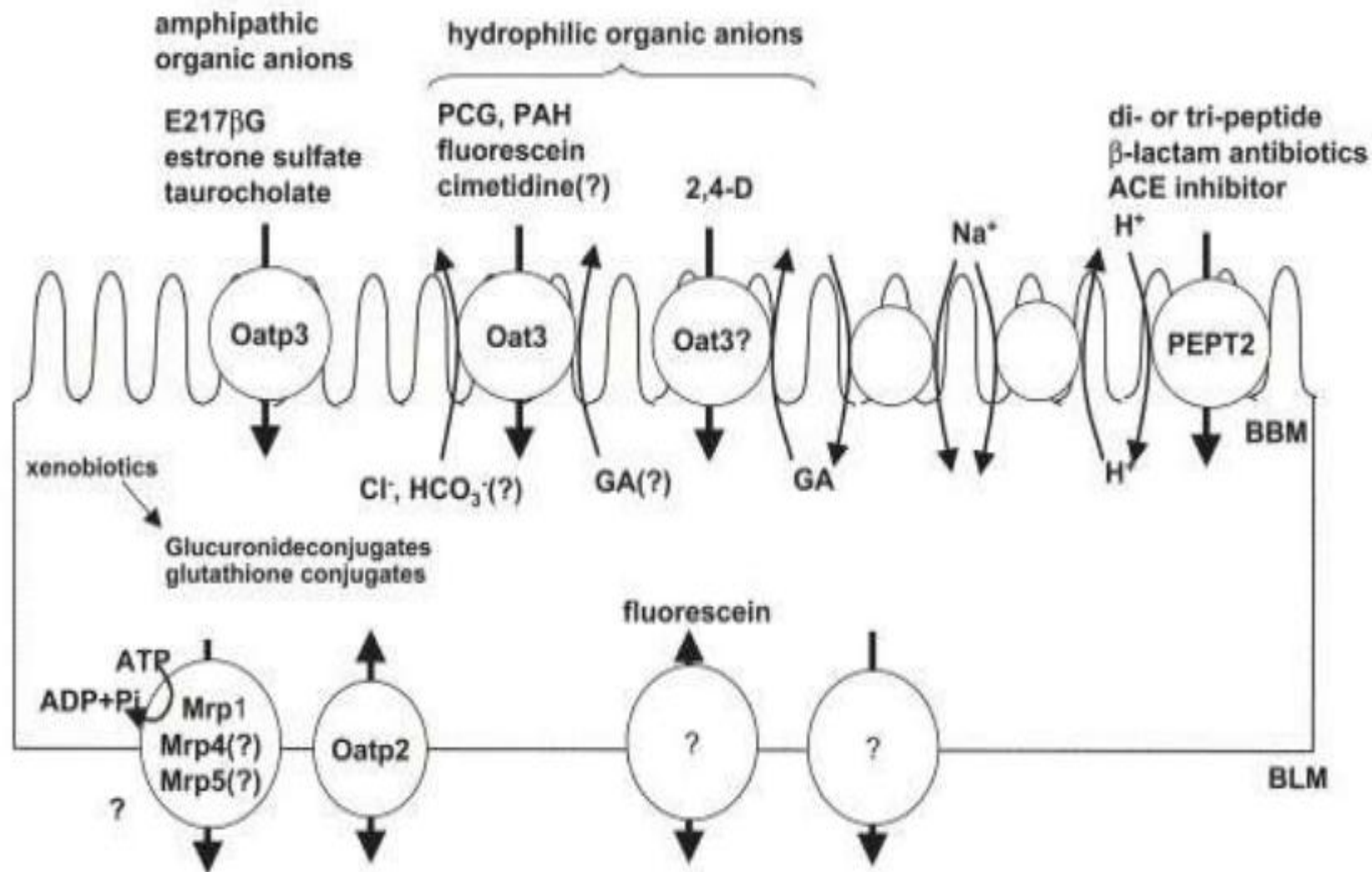
- Organic anion transporters are classified into
 1. Organic anion transporters (OATs)
 2. Organic anion transporting polypeptides (OATPs)
 3. Multiple drug resistance-associated proteins (MRPs)

Organic anion transporters (OAT)



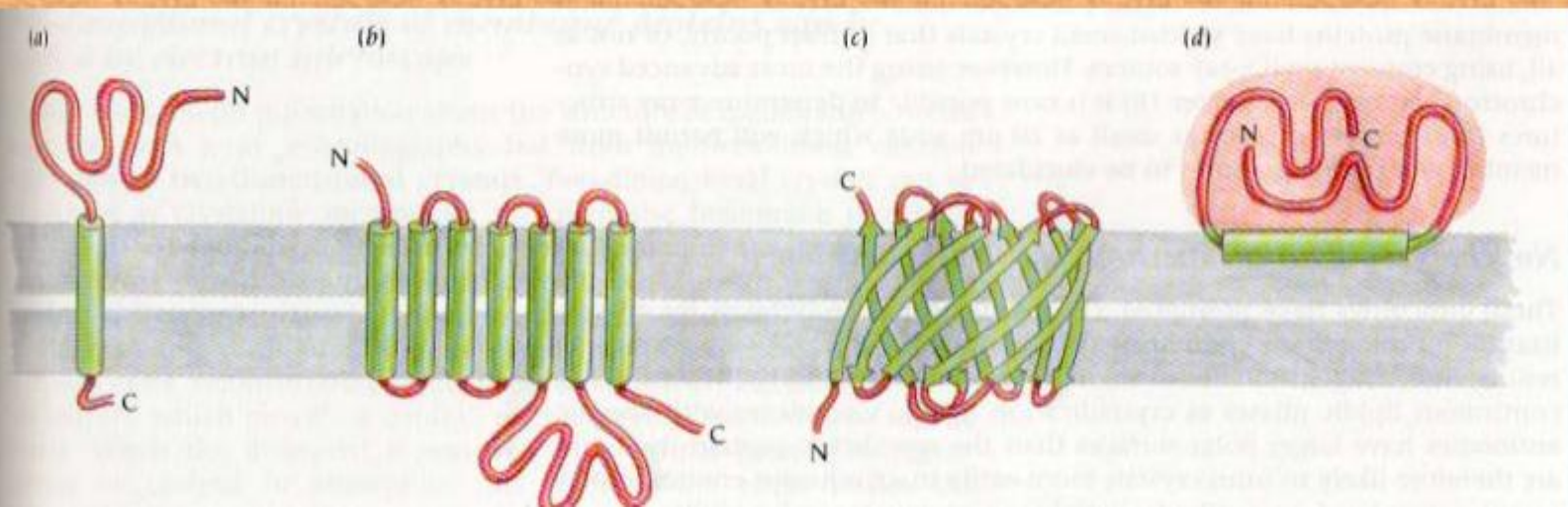
- Five structurally related isoforms i.e. OAT 1-OAT 5 have been identified.
- These are expressed in the kidney and have important functions in renal clearance.
- OAT2 is expressed at higher levels in liver as compared to kidney.
- OATs are also expressed to a lesser extent in brain, muscle, eye and placenta.

CSF-side



Blood-side

- Topology characteristics include twelve 12 α -helix two transmembrane domains (TMD), one large hydrophilic extracellular loop between TMD 1 and TMD 2 carrying glycosylation sites and a large intracellular loop containing multiple phosphorylation sites between TMD 6 and TMD 7.



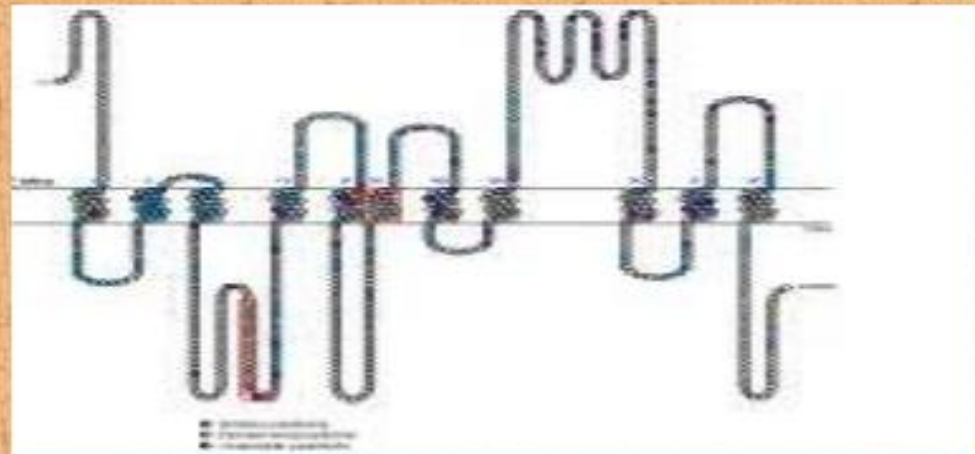


- OATs are **polyspecific transporters** that interact with various clinically significant organic anion drugs such as
- Non steroidal anti-inflammatory drugs (**NSAIDs**), β -lactam antibiotics, antiviral drugs, diuretics, **antitumor drugs** and **angiotensin-converting enzyme inhibitors** .
- The role of OAT family in the **intestinal absorption of drugs seems negligible** because they have not been identified in human intestine.

Organic anion transporting polypeptides (OATPs)



- OATPs are the rapidly expanding family of mammalian transporters and transport a wide range of **amphipathic endogenous and exogenous organic compounds**.
- The topology include twelve TMD containing a large extracellular domain with multiple glycosylation sites.





- OATP mediate transmembrane transport of wide range of organic compounds
 1. **organic anions**, such as bromosulfophthalein (BSP), bile salts, bilirubin, prostaglandins, and estrogen-conjugates;
 2. **neural steroids and steroid conjugates**;
 3. **lipophilic organic cations**, e.g., rocuronium; and
 4. **organic dyes**, thyroid hormones, and anionic oligopeptides.
- Various **pharmaceutically relevant compounds** such as digoxin, pravastatin, methotrexate, temocaprilat, benzylpenicillin, fexofenadine, (D-Pen2, D-Pen5)-enkephalin (DPDPE), as well as some NSAIDs.



- Mechanism driving OATP mediated transport are
 1. Na^+ -independent manner
 2. Anion exchange mechanism
 3. Glutathione substrate transport
 4. Proton-coupled transport mechanism



- Expression of OATPs (OATP-C and OATP-8 occur at the basolateral membrane of hepatocytes
- While other OATPs like OATP-B, OATP-D and OATP-E are fairly expressed in tissues including blood-brain barrier, lung, heart, kidney, placenta and intestine.
- The regulation of OATPs expression and functional kinetics can occur at both transcriptional and post-transcriptional levels.

